

## **TITLE - Inflammation and haemostatic dysfunction; novel risk factors for cognitive decline in older patients with vascular risk factors or disease**

### **Researchers**

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### **Aim**

To determine whether activated blood clotting (haemostasis) in older people is associated with decline in cognition (ability to think) and increased risk of disability.

### **Project Outline/Methodology**

We analysed blood samples from 5,804 people aged 70-82 years, who were randomised to receive the cholesterol-lowering drug pravastatin or placebo in the PROSPER study (Prospective Study of Pravastatin in the Elderly at Risk). Mean follow-up was for 3.2 years, with annual measurement of speed of information processing (Letter Digit Coding and Stroop test), immediate and delayed memory (Picture-word naming and general cognitive function (Mini-Mental State Examination) and activities of daily living.

### **Key Results**

We found that impaired cognitive function in older people was associated with increases in measures of thrombin generation (a key component of blood clotting), plasma viscosity (thicker sticky blood) and tissue plasminogen activator (a marker of damage to blood vessel walls – associated with increased risk of blood clotting). In addition, more rapid rate of cognitive decline was seen with increased levels of tests of thrombin generation, particularly the specific measure, D-dimer. More rapid decline in activities of daily living was also observed with all aspects of activated blood clotting. Strokes and heart attacks explained only part of this decline. Inflammation appeared to play only a modest role in contributing to the associations of blood clotting markers with decline in cognition and activities of daily living.

### **Conclusions**

Older patients with activation of thrombin generation tend to have poorer cognitive function and are at increased risk of more rapid cognitive decline. Increased thrombin generation, sticky blood, and

damage to blood vessel walls also are associated with more rapid decline in activities of daily living.

It is likely that circulation problems, including increased blood clotting, play a major role in mental and physical decline in older age. These circulation problems are often not recognised as strokes or heart attacks.

### **What does this study add to the field?**

This is the first large-scale longitudinal study (following up patients over a period of time) to have examined a wide range of markers of blood clotting in relation to cognitive decline in older people, and the first to explore the potential link with disability.

### **Implications for Practice or Policy**

Prevention of cognitive decline, dementia and disability in older age is a major priority for healthcare. To-date there are few data to guide and rationalise interventions that are most likely to achieve these health gains. From our study plausible targets are inhibition of thrombin generation, including lifestyle modification such as regular exercise and smoking cessation, and selective use of drugs such as thrombin inhibitors in high-risk subgroups.

### **Where to next?**

Studies are planned with extended follow-up of the PROSPER cohort, including use of routine health statistics and re-contacting subjects to determine longer term cognitive outcomes and incident disability. This will allow us to determine the link between blood clotting, dementia and more severe disability. Annual brain Magnetic Resonance Image scans were performed in a subgroup of the study, and these will be used to look for possible links between blood clotting and progressive circulation damage to the brain.

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